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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,276	08/27/1999	HIDEAKI TADA	Q55589	2406

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	24

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/380,276	TADA ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on May 19, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/320,276 is acceptable and a CPA has been established. An action on the CPA follows.

Status of Claims

2. Claims 1-8 and 11-22 are pending in the instant application. Claims 8 and 22 have been amended and claims 9 and 10 have been canceled as requested by Applicant in Paper Number 23, filed May 19, 2003.

All claims are currently under examination.

Withdrawn Claim Objections

3. The objection to the claims is withdrawn in view of Applicants' amendment.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-8 and 1-22 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility,

for reasons of record in the previous Office Actions, Paper No.11 at pages 3-6, Paper No. 16, at pages 3-5, and Paper No. 20, and below.

Applicants traverse the rejection and submit on pages 6-7 of the response that in the Amendment dated December 17, 2002, Applicants asserted that both the TAJ protein (Eby et al.) and the protein of the present invention are substantially the same, the protein of the present application has the same function and activity as the TAJ protein, namely the ability to induce cell death, and that Applicants also discussed support in the specification for the cell death inducing activity of the present invention.

Applicants assert that for example, at page 17, lines 6-10, it is stated that the polypeptide of the present invention will show biological activities including cell death, and that this activity is supported in the disclosure of Eby et al. Applicants disagree with the Examiner that the TAJ protein has specific tissue expression, and such expression is not supported by the specification, by asserting that as discussed throughout Eby et al, the primary activity for the TAJ protein in predicted to be in embryonic development, and this activity is fully supported in the specification, point to pages 18, 19 and 20, which discuss cell proliferation and differentiation activities on erythroid progenitor cells, myeloid cells, megakaryocytes and hematopoietic cells, and on page 29, which discusses the involvement of the protein of the instant invention in embryonic development. Applicants also assert that while it is disclosed in Eby et al. that the TAJ protein is expressed in the prostate gland, a role for the protein in this gland is not discussed or predicted in the publication.

Applicants' arguments have been fully considered but are not deemed persuasive. The central issue is whether or not the asserted activity of the protein, the ability to induce cell death,

is a patentable utility, and is supported by the specification as filed. While the instant application discusses the possible role of the protein of the instant invention in apoptosis, it also describes other activities which are based solely on the protein belonging to the TNF family of receptors. On page 17, lines 1-12, it is stated:

> "Since repetitive structures of Cys are present at three points in the extracellular domain of the polypeptide of the invention, it is obvious that this is a novel protein belonging to the TNF receptor family and exerts its activity via a ligand belonging to a known or unknown TNF family. In consequence, it is considered that the polypeptide of the invention and a cDNA molecule which encodes the polypeptide will show one or more of the effects or biological activities (including those which relates to the assays cited below) concerning differentiation, proliferation, growth, survival or cell death of hematopoietic, immune and nerve system cells, immune system functions, proliferation and growth of tumor, inflammations, bone metabolism, etc."

The specification also describes a myriad number of activities, diseases or disorders which are associated with the molecules of the instant invention, such as cytokine activity, immune stimulating/suppressing activity, hematopoiesis regulation activity, tissue generation/regeneration activity, activin/inhibin activity, chemotactic/chemokinetic activity, hemostatic and thrombolytic activity (pages 18-26), as well as other activities such as enhancing or suppressing bodily characteristics such as height, weight, hair color, tissue pigmentation, effecting behavioral characteristics including cognition, depression and violent behaviors (page 27), and it is asserted in the specification on page 29 that the protein of the instant invention is expected during embryogenesis to promote or inhibit the organogenesis of epidermis, brain backbone, and nervous system by induction of ectoderm, that of notochord connective tissues (bone, muscle, tendon), hemocytes, heart, kidney and genital organs by induction of mesoderm,

and that of digestive apparatus (stomach, intestine, liver, pancreas), respiratory apparatus (lung, trachea) by induction of endoderm, and in adult, also, this polypeptide is thought to proliferate or inhibit the above organs. A number of diseases or disorders also associated with the molecules of the instant invention are listed on pages 29-32.

Although homology to the TNF receptor family and expression provides evidence that the claimed protein is a member of the TNF receptor superfamily, it is not predictable what the function of the proteins of the instant invention are from this information. Whereas a broad class of enzyme such as the ligases have a general utility in such an application as ligation of DNA for cloning purposes and which is essentially applicable to all of the members of that class, the class of proteins known as TNF receptors do not have a common practical utility which is based upon a property common to all of the members of that class. Members of this superfamily bind to a large variety of different ligands, mediates different signals, are expressed in different cell types and modulate different physiological processes, and are involved in different diseases and/or disorders, and it is not predictable what the specific physiological function of a TNF receptor is based on homology to other members of this family (Wallach, D. (2000) TNF ligand and TNF/NGF receptor families. In: Cytokine Reference (Joost J. Oppenheim and Marc Feldmann editors in chief, Academic Press (London), 377-411). Though the protein of the instant invention may be classified as a member of the TNF receptor superfamily, this does not automatically confer a specific and substantial utility to the protein, since there is diversity in the activities and biological functions of these receptors.

Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001, where on page 1096, third column, it is stated:

"For example, where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class."
The receptors of the instant invention fall into this category.

Even though it is stated that the protein of the instant invention can cause cell death and Erby et al. teaches that overexpression (in some cells) causes apoptosis, this is not a patentable utility. It is not disclosed in what cells, and under what conditions, the protein of the instant invention is involved in. One of ordinary skill in the art would not know how to use the molecules of the instant invention except for further research to discover it's role in apoptosis. At least one specific and substantial activity must be disclosed. The Revised Interim Utility Guidelines Training Materials state "Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." The polypeptides of the instant invention would require substantial further research to determine how they could be used or if they were involved in any disease state.

The proposed use of the claimed invention is simply a starting point for further research and investigation into practical uses of the protein. This further experimentation is a useful in basic research, but does not constitute a specific, substantial or well-established utility.
As the Supreme Court said in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct. 1966):

> "A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Applicants also assert that based on the disclosed activities of the present invention, supported by Eby et al., that skilled artisan would readily understand that a polypeptide involved

in the induction of cell death could be used in a number of important manners, for example, a specific and substantial utility could be had in the preparation of an agent for treating or diagnosing diseases caused by uncontrolled cell death induced by the aberrant expression of the protein of the present invention.

Applicants' arguments have been fully considered but are not deemed persuasive. ***If*** the protein of the instant invention was found to be aberrantly expressed in a specific disease or disorder, this could possibly result in a patentable utility for the protein. However, there is no nexus between the protein of the instant invention and any disease or disorder. A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polypeptides or polynucleotides to treat/and or diagnose a particular disease; it merely defines a starting point for further research and investigation. Therefore, the rejection based on 35 U.S.C. § 101 is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8 and 11-22 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of how to use the particularly disclosed polypeptides, enablement would not be found commensurate in scope with the claims. Even if there were a patentable use for the proteins of SEQ ID NOS: 4 and 8,

variants of 95% identity would not be enabled because the specification has not taught one of ordinary skill in the art how to use them. The specification has not provided guidance on how to make and use a polypeptide comprising an amino acid sequence having at least 95% identity with amino acids of SEQ ID NO: 4 or 8 without undue experimentation. There are no motifs identified that are critical to function, and it is not predictable how any given set of amino acid changes will affect the protein's activity, and no functional limitation in the claims. Therefore, the rejection based on 35 U.S.C. § 112 first paragraph is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Eileen B. O'Hara

Patent Examiner